

# NMCP COVID-19 Literature Report #83: Friday, 17 December 2021

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**Purpose:** These reports, published every other week on Fridays, are curated collections of current research, evidence reviews, special reports, grey literature, and news regarding the COVID-19 pandemic that may be of interest to medical providers, leadership, and decision makers. Please reach out with questions, suggestions for future topics, or any other feedback.

All reports are available online at <https://nmcp.libguides.com/covidreport>. Access is private; you will need to use the direct link or bookmark the URL.

**Disclaimer:** I am not a medical professional. This document is current as of the date noted above. While I make every effort to find and summarize available data, I cannot cover everything in the literature on COVID-19. Due to the rapid evolution of the literature, I will not update past reports when new information arises; for retracted papers specific to COVID-19, see the [list of retracted papers from Retraction Watch](#).

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## **The Big Picture**

### ***News in Brief***

The US has reached 800,000 coronavirus-related deaths; "[t]he milestone means the U.S. death toll from this one virus now exceeds the entire population of North Dakota" ([Reuters](#)).

The US has also crossed 50 million cases ([Reuters](#)).

"Two years into this pandemic, the world is dangerously unprepared for the next one, report says" ([WP](#); see also: [GHS Index report](#)).

For some literal big pictures, see: "The best science images of 2021 — a helicopter on Mars, human–monkey embryos, volcanic ash and more" ([Nature](#)).

### ***Special Reports and Other Resources***

CSIS: Building [Apollo's Arsenal: Acquiring Covid-19's Lessons Learned for Government - Bioeconomy Partnership](#) (14 December 2021)

"This brief concludes the CSIS Defense-Industrial Initiative Group's series on enhancing future biosecurity, examining three cross-national case studies and aspects of the U.S. response, to provide lessons learned from the overall project. The case studies include aspects of three government responses to the Covid-19 pandemic: South Korea's strategy for testing and diagnostics, New Zealand's strategy for data management, and China's strategy for laboratory research. The brief then examines aspects of current U.S. government biosecurity preparations and responses, including the flagship Apollo Project. Lessons learned highlight the importance of accessible, effective data management for both biosurveillance and dispatching supplies to outbreak hotspots. The bioeconomy has the potential to act as surge capacity and innovation reservoir—if mechanisms for coordination and production are established ahead of crisis periods to take advantage of this resource. Likewise, biosecurity research and development (R&D) is a peacetime priority to ensure that resources are ready when they are needed: biosecurity-related defense R&D spending remained relatively flat through the first year of the Covid-19 pandemic, demonstrating that many of the technologies that turned the tide of a pandemic were developed over the years and decades before."

BPC: [Public Health Forward: Modernizing the U.S. Public Health System](#) (December 2021)

"The COVID-19 pandemic has made clear that the nation's health, safety, and economic prosperity depends on its ability to minimize the effects of devastating public health threats. The nation's resilience to current and future public health threats is largely dependent upon a modern U.S. public health system of state and local health departments

that have the resources, capacities, and workforce to protect and promote health for all Americans.

Join the Bipartisan Policy Center, national public health associations, and philanthropic foundations as they release a report from the bipartisan Public Health Forward Task Force establishing a 5-year vision for governmental public health in the U.S. and an actionable framework for state and local elected and public health officials to enhance public health infrastructure."

Includes video and report on proceedings.

JHCHS: [Integrating Primary Care and Public Health to Save Lives and Improve Practice During Public Health Crises: Lessons from COVID-19](#) (14 December 2021)

"As of September 2021, mortality in the United States due to the SARS-CoV-2 virus had exceeded the death toll from the 1918 influenza pandemic. COVID-19 was the ultimate test of healthcare and public health capacity and capability across the United States. From its acute onset and throughout its extended duration, the COVID-19 pandemic has overwhelmed hospitals, disrupted businesses, and caused lasting economic harm. It has also illuminated and exploited major vulnerabilities within the US healthcare and public health systems. The impact of the pandemic on hospitals, and to a lesser extent on public health departments, has been explored elsewhere, but relatively little has been written about the impact on primary care services. Operating largely in silos and chronically underfunded disciplines, primary care providers and public health practitioners in the United States have struggled to respond to the numerous waves of the pandemic, which have caused high levels of morbidity and mortality and jeopardized health systems in communities across the country, especially those that are most vulnerable. It is crucial that the lessons learned from the COVID-19 pandemic must be shared.

To explore the degree of collaboration that has occurred among primary care and public health providers during the pandemic to date, we used a mixed-method, rapid-cycle approach, which included a literature review and key informant interviews. We interviewed primary care providers at family medicine and general internal medicine practices in integrated health systems and federally qualified health centers, personnel at the National Association of Community Health Centers, and state and local public health officials across several states about COVID-19 activities and lessons learned.

The findings of this study demonstrate that the failure to bring primary care providers into a frontline role as responders, alongside public health, resulted in many missed opportunities to provide better quality care, faster testing, more effective contact tracing, greater acceptance of vaccination, and better communication with patients. Participants in this study further indicated that better integration of primary care, public health, and community-based organizations could have provided greater support for the public health

response, thereby easing the burden on overstretched public health personnel; and could have accessed primary care's reach to amplify public health messaging. If these coordinated activities had been effectively implemented, they could have saved lives and reduced the health, economic, and societal impact of the pandemic in the United States.

This study reveals the extraordinary burden primary care and public health faced in meeting the demands created by a rapidly evolving severe pandemic, while simultaneously attempting to address the normal healthcare needs of existing patients and families. The level of preparedness to respond swiftly and effectively to the COVID-19 pandemic varied widely across public health and primary care organizations. In the key informant interviews, we found that the most productive collaborations during the COVID-19 response tended to be extensions of preexisting relationships between public health and primary care personnel or 'test and treat' and other disease management models. Workforce flexibility and adaptability and the expansion of telehealth services were also central themes in these interviews. Federally qualified health centers played a critical role and pivoted quickly and effectively to provide both primary care and public health interventions during the COVID-19 pandemic, particularly those that serve higher-risk populations.

The data and themes described in this report clearly indicate that the COVID-19 pandemic must be a catalyst for change. The landscape of primary care in the United States is rapidly evolving; many traditional practices are being acquired by integrated health systems and for-profit companies and other practices are abandoning traditional fee-for-service reimbursement models in favor of various forms of capitation or prepayment. In light of these changes, now may be an opportune time to encourage better alignment and collaboration with public health.

Recognizing that high-quality primary care is the foundation of a healthcare system and that a robust public health system is the bedrock for healthy communities, we conclude that action is needed to address the barriers that exist between primary care and public health and to correct misalignment across systems. A new transformative vision is needed where public health is central to the delivery of healthcare in the US and where local primary care, public health, and community networks are strengthened and expanded. While payment reform is critical, action will be required by primary care and public health leadership and policymakers to build and sustain a thriving, resilient, integrated primary care, public health, and community sectors capable of optimizing health outcomes during future pandemics and large-scale public health emergencies. We make the following key recommendations:

- Colocate primary care and public health services to benefit population-level health and facilitate active collaboration.
- Primary care societies must align their efforts with public health in a unified voice to drive congressional action in order to ensure that the disastrous response to the COVID-19 pandemic is not repeated.

- Craft efforts to support, protect, and sustain the primary care and public health workforces to drive integration across disciplines.
- Public health 'moves at the speed of trust' and people trust their primary care providers and community-based organizations; therefore, primary care and public health collaborative partnerships with strong ties to their community organizations should enhance health systems surge capacity, extend public health disease containment interventions, and position the United States for improved response to future pandemic."

## **SARS-CoV-2 Virus and Variants**

### ***News in Brief***

#### *Variant of Concern: Omicron*

"Latest on omicron variant and COVID-19 vaccine protection" ([NIH](#)).

"Understanding omicron's many mutations. The virus's spikes have far more changes than we've seen in any previous variant, and researchers are racing to figure out how they affect it — and us" ([WP](#)).

"The Omicron variant can likely outcompete Delta — and that could worsen the U.S. Covid-19 epidemic" ([STAT](#)).

Listen: "Omicron — your questions answered" ([Coronapod](#)).

#### *Omicron: The Basics*

"Omicron variant more resistant to vaccine but causes less severe covid, major South African study concludes" ([WP](#)).

"Waning COVID super-immunity raises questions about Omicron" ([Nature](#)).

"While the Omicron variant is not the common cold, a pre-print found the two viruses may share some of the same genetic material" ([Medpage](#); see: [preprint at OSF](#)).

"Preliminary laboratory data hint at what makes Omicron the most superspreading variant yet" ([STAT](#)).

#### *Omicron: Transmission*

"Omicron spreads faster than any other variant, WHO says. It's now in 77 countries" ([NPR](#)).

"Omicron spreading rapidly in U.S. and could bring punishing wave as soon as January, CDC warns" ([WP](#)).

"Lung tissue study sheds light on fast Omicron spread" ([CIDRAP](#)).

### *Tracking Variants*

"Genomic surveillance data indicates the omicron COVID-19 variant accounts for about 3 percent of new U.S. cases" ([BHR](#)).

"Omicron could soon become dominant in some European countries, officials predict" ([WP](#)).

"Omicron blindspots: why it's hard to track coronavirus variants" ([Nature](#)).

"Scientists find 'stealth' version of Omicron that may be harder to track" ([Guardian](#)).

### *Long Reads*

"America is not ready for omicron: The new variant poses a far graver threat at the collective level than the individual one—the kind of test that the U.S. has repeatedly failed" ([Atlantic](#)).

"Beyond Omicron: what's next for COVID's viral evolution — the rapid spread of new variants offers clues to how SARS-CoV-2 is adapting and how the pandemic will play out over the next several months" ([Nature](#)).

### ***Special Reports and Other Resources***

WHO: [Enhancing Readiness for Omicron \(B.1.1.529\): Technical Brief and Priority Actions for Member States](#) (10 December 2021)

"On 26 November 2021, WHO designated the variant B.1.1.529 a variant of concern (VOC), on the basis of advice from WHO's Technical Advisory Group on Virus Evolution. The variant has been given the name Omicron. Omicron variant is a highly divergent variant with a high number of mutations, including 26-32 in the spike protein, some of which are concerning and may be associated with immune escape potential and higher transmissibility. However, there are still considerable uncertainties. As of 9 December 2021, cases of human infections with this variant have been identified in 63 countries across all six WHO regions. Current understanding of the Omicron variant from recent data are likely to evolve as more data becomes available.

The overall threat posed by Omicron largely depends on three key questions, including: (1) how transmissible the variant is; (2) how well vaccines and prior infection protect against infection, transmission, clinical disease and death; and (3) how virulent the variant is compared to other variants. Public health advice is based on current information and will be tailored as more evidence emerges around those key questions.

Based on current limited evidence Omicron appears to have a growth advantage over Delta. It is spreading faster than the Delta variant in South Africa where Delta circulation was low, but also appears to spread more quickly than the Delta variant in other countries where the incidence of Delta is high, such as in the United Kingdom. Whether Omicron's observed rapid growth rate in countries with high levels of population immunity is related to immune evasion, intrinsic increased transmissibility, or a combination of both remains uncertain. However, given the current available data, it is likely that Omicron will outpace the Delta variant where community transmission occurs.

There are still limited data on the clinical severity of Omicron. While preliminary findings from South Africa suggest it may be less severe than Delta, and all cases reported in the EU/EEA to date have been mild or asymptomatic, it remains unclear to what extent Omicron may be inherently less virulent. More data are needed to understand the severity profile.

There are limited available data, and no peer-reviewed evidence, on vaccine efficacy or effectiveness to date for Omicron. Preliminary evidence, and the considerably altered antigenic profile of the Omicron spike protein, suggests a reduction in vaccine efficacy against infection and transmission associated with Omicron. There is some preliminary evidence that the incidence of reinfection has increased in South Africa, which may be associated with humoral (antibody-mediated) immune evasion. In addition, preliminary evidence from a few studies of limited sample size have shown that sera obtained from vaccinated and previously infected individuals had lower neutralization activity (the size of the reduction ranges considerably) than with any other circulating VOCs of SARS-CoV-2 and the ancestral strain.

The diagnostic accuracy of routinely used PCR and antigen-based rapid diagnostic test (Ag-RDT) assays does not appear to be influenced by Omicron. Most Omicron variant sequences reported include a deletion in the S gene, causing some S gene targeting PCR assays to appear negative. Although some publicly shared sequences lack this deletion, this remains a minority of currently available sequences, and S gene target failure (SGTF) can therefore be used as a useful proxy marker of Omicron, for surveillance purposes. However, confirmation should be obtained by sequencing, as this deletion can also be found in other VOCs (e.g., Alpha and subsets of Gamma and Delta).

Therapeutic interventions for the management of patients with severe or critical COVID-19 associated with the Omicron variant that target host responses (such as corticosteroids, and interleukin 6 receptor blockers and prophylaxis with anticoagulation) are expected to remain effective. However, monoclonal antibodies will need to be tested individually, for their antigen binding and virus neutralization and these studies should be prioritized."

## ***Journal Articles***

MMWR: [SARS-CoV-2 B.1.1.529 \(Omicron\) Variant — United States, December 1–8, 2021](#) (17 December 2021)

"What is already known about this topic? SARS-CoV-2 variant B.1.1.529 (Omicron), first reported to WHO on November 24, 2021, has been designated a variant of concern. Mutations in Omicron might increase transmissibility, confer resistance to therapeutics, or partially escape infection- or vaccine-induced immunity.

What is added by this report? During December 1–8, 2021, 22 U.S. states reported at least one COVID-19 case attributed to the Omicron variant. Among 43 cases with initial follow-up, one hospitalization and no deaths were reported.

What are the implications for public health practice? Implementation of concurrent prevention strategies, including vaccination, masking, improving ventilation, testing, quarantine, and isolation are recommended to slow transmission of SARS-CoV-2, including variants such as Omicron, to protect against severe illness and death from COVID-19."

Clin Infect Dis: [Neutralization of SARS-CoV-2 Omicron variant by sera from BNT162b2 or Coronavac vaccine recipients](#) (16 December 2021)

"Background: The SARS-CoV-2 Omicron variant, designated as a Variant of Concern(VOC) by the World Health Organization, carries numerous spike mutations which have are known to evade neutralizing antibodies elicited by COVID-19 vaccines. A deeper understanding of the susceptibility of Omicron variant to vaccine-induced neutralizing antibodies is urgently needed for risk assessment.

Methods: Omicron variant strains HKU691 and HKU344-R346K were isolated from patients using TMPRSS2-overexpressing VeroE6 cells. Whole genome sequence was determined using nanopore sequencing. Neutralization susceptibility of ancestral lineage A virus and the Omicron, Delta and Beta variants to sera from 25 BNT162b2 and 25 Coronavac vaccine recipients was determined using a live virus microneutralization assay.

Results: The Omicron variant strain HKU344-R346K has an additional spike R346K mutation, which is present in 8.5% of strains deposited in GISAID database. Only 20% and 24% of BNT162b2 recipients had detectable neutralizing antibody against the Omicron variant HKU691 and HKU344-R346K, respectively, while none of the Coronavac recipients had detectable neutralizing antibody titer against either Omicron isolate. For BNT162b2 recipients, the geometric mean neutralization antibody titers(GMT) of the Omicron variant isolates(5.43 and 6.42) were 35.7-39.9-fold lower than that of the ancestral virus(229.4), and the GMT of both Omicron variant isolates were significantly lower than those of the Beta and Delta variants. There was no significant difference in the GMT between HKU691 and HKU344-R346K.

Conclusions: Omicron variant escapes neutralizing antibodies elicited by BNT162b2 or Coronavac. The additional R346K mutation did not affect the neutralization susceptibility. Our data suggest that the Omicron variant may be associated with lower COVID-19 vaccine effectiveness."

Clin Infect Dis: [Host predictors of broadly cross-reactive antibodies against SARS-CoV-2 variants of concern differ between infection and vaccination](#) (10 December 2021)

"Background: Following SARS-CoV-2 infection or vaccination there is significant variability between individuals in protective antibody levels against SARS-CoV-2, and within individuals against different virus variants. However, host demographic or clinical characteristics that predict variability in cross-reactive antibody levels are not well-described. These data could inform clinicians, researchers, and policy makers on the populations most likely to require vaccine booster shots.

Methods: In an institutional review board-approved prospective observational cohort study of staff at St. Jude Children's Research Hospital, we identified participants with plasma samples collected after SARS-CoV-2 infection, after mRNA vaccination, and after vaccination following infection, and quantitated IgG levels by ELISA to the spike receptor binding domain (RBD) from five important SARS-CoV-2 variants (Wuhan Hu-1, B.1.1.7, B.1.351, P.1 and B.1.617.2). We used regression models to identify factors that contributed to cross-reactive IgG against one or multiple viral variants.

Results: Following infection, a minority of the cohort generated cross-reactive antibodies, IgG antibodies that bound all tested variants. Those that did had increased disease severity, poor metabolic health, and were of a particular ancestry. Vaccination increased the levels of cross-reactive IgG levels in all populations including immunocompromised, elderly and persons with poor metabolic health. Younger people with a healthy weight mounted the highest responses.

Conclusions: Our findings provide important new information on individual antibody responses to infection/vaccination that could inform clinicians on the populations that may require follow-on immunization."

Clin Infect Dis: [Duration of SARS-CoV-2 Natural Immunity and Protection against the Delta Variant: A Retrospective Cohort Study](#) (03 December 2021)

"Background: Infection with SARS-CoV-2 has been shown to be highly protective against reinfection and symptomatic disease. However, effectiveness against the highly transmissible Delta variant and duration of natural immunity remain unknown.

Methods: This retrospective cohort study included 325,157 patients tested for coronavirus disease 2019 (COVID-19) via polymerase chain reaction (PCR) from 09 March 2020 to 31 December 2020 (Delta variant analysis) and 152,656 patients tested from 09 March 2020 to

30 August 2020 (long-term effectiveness analysis) with subsequent testing through 09 September 2021. The primary outcome was reinfection, defined as a positive PCR test >90 days after initial positive test.

Results: Among 325,157 patients tested before 31 December 2020, 50,327 (15.5%) tested positive. After 01 July 2021 (Delta dominant period), 40 (0.08%) of the initially positive and 1,494 (0.5%) of the initially negative patients tested positive. Protection of prior infection against reinfection with Delta was 85.4% (95% CI, 80.0-89.3). For the long-term effectiveness analysis, among 152,656 patients tested before 30 August 2020, 11,186 (7.3%) tested positive. After at least 90 days, 81 (0.7%) of the initially positive patients and 7,167 (5.1%) of the initially negative patients tested positive. Overall protection of previous infection was 85.7% (95% CI, 82.2-88.5) and lasted up to 13 months. Patients over age 65 had slightly lower protection.

Conclusions: SARS-CoV-2 infection is highly protective against reinfection with the Delta variant. Immunity from prior infection lasts for at least 13 months. Countries facing vaccine shortages should consider delaying vaccinations for previously infected patients to increase access."

## COVID-19 Vaccines

### *News in Brief*

"J&J's COVID vaccine on the way out? CDC panel demotes vaccine but stops short of recommending against use" ([Medpage](#)).

"How COVID vaccines shaped 2021 in eight powerful charts" ([Nature](#)).

"German police move against an alleged murder plot by anti-vaccination extremists" ([NPR](#)).

Visual data: "The uneven Covid-19 vaccine rollout" ([Statista](#)).

### *Military*

"Vaccine holdouts in U.S. military approach 40,000 even as omicron variant fuels call for boosters" ([WP](#)).

The Air Force discharged 27 ([AP](#)), 103 Marines were discharged and the Army has relieved 6 leaders ([Politico](#)) for refusal to get COVID vaccine.

### ***Special Reports and Other Resources***

Commonwealth Fund: [The U.S. COVID-19 Vaccination Program at One Year: How Many Deaths and Hospitalizations Were Averted?](#) (14 December 2021)

"In the absence of a vaccination program, there would have been approximately 1.1 million additional COVID-19 deaths and more than 10.3 million additional COVID-19 hospitalizations in the U.S. by November 2021.

Without the U.S. vaccination program, COVID-19 deaths would have been approximately 3.2 times higher and COVID-19 hospitalizations approximately 4.9 times higher than the actual toll during 2021.

If no one had been vaccinated, daily deaths from COVID-19 could have jumped to as high as 21,000 per day — nearly 5.2 times the level of the record peak of more than 4,000 deaths per day recorded in January 2021."

### ***Journal Articles***

MMWR: [Report of Health Care Provider Recommendation for COVID-19 Vaccination Among Adults, by Recipient COVID-19 Vaccination Status and Attitudes — United States, April–September 2021](#) (17 December 2021)

"What is already known about this topic? COVID-19 vaccination is critical to controlling the COVID-19 pandemic; health care providers play an important role in achieving high vaccination coverage.

What is added by this report? Adults who reported a provider COVID-19 vaccination recommendation were more likely to have been vaccinated, to be concerned about COVID-19, to have confidence that COVID-19 vaccines are important and safe, and to perceive that family and friends had been vaccinated.

What are the implications for public health practice? A health care provider recommendation for COVID-19 vaccines at every visit could increase coverage and confidence in vaccines, particularly among groups with lower COVID-19 vaccination coverage, including younger adults, racial/ethnic minorities, and rural residents."

### ***Efficacy and Immune Response***

JAMA Netw Open: [Estimated Effectiveness of COVID-19 Messenger RNA Vaccination Against SARS-CoV-2 Infection Among Older Male Veterans Health Administration Enrollees, January to September 2021](#) (15 December 2021)

"This case-control study examines estimated COVID-19 messenger RNA vaccination effectiveness against SARS-CoV-2 infection from January to September 2021 among fully vaccinated male veterans aged 65 years or older."

NEJM: [Efficacy and Safety of NVX-CoV2373 in Adults in the United States and Mexico](#) (15 December 2021)

"Background: NVX-CoV2373 is an adjuvanted, recombinant spike protein nanoparticle vaccine that was shown to have clinical efficacy for the prevention of coronavirus disease 2019 (Covid-19) in phase 2b-3 trials in the United Kingdom and South Africa, but its efficacy had not yet been tested in North America.

Methods: We conducted a phase 3, randomized, observer-blinded, placebo-controlled trial in the United States and Mexico during the first half of 2021 to evaluate the efficacy and safety of NVX-CoV2373 in adults ( $\geq 18$  years of age) who had not had severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Participants were randomly assigned in a 2:1 ratio to receive two doses of NVX-CoV2373 or placebo 21 days apart. The primary objective was to determine vaccine efficacy against reverse-transcriptase-polymerase-chain-reaction-confirmed Covid-19 occurring at least 7 days after the second dose. Vaccine efficacy against moderate-to-severe disease and against different variants was also assessed.

Results: Of the 29,949 participants who underwent randomization between December 27, 2020, and February 18, 2021, a total of 29,582 (median age, 47 years; 12.6%  $\geq 65$  years of age) received at least one dose: 19,714 received vaccine and 9868 placebo. Over a period of 3 months, 77 cases of Covid-19 were noted - 14 among vaccine recipients and 63 among placebo recipients (vaccine efficacy, 90.4%; 95% confidence interval [CI], 82.9 to 94.6;  $P < 0.001$ ). Ten moderate and 4 severe cases occurred, all in placebo recipients, yielding vaccine efficacy against moderate-to-severe disease of 100% (95% CI, 87.0 to 100). Most sequenced viral genomes (48 of 61, 79%) were variants of concern or interest - largely B.1.1.7 (alpha) (31 of the 35 genomes for variants of concern, 89%). Vaccine efficacy against any variant of concern or interest was 92.6% (95% CI, 83.6 to 96.7). Reactogenicity was mostly mild to moderate and transient but was more frequent among NVX-CoV2373 recipients than among placebo recipients and was more frequent after the second dose than after the first dose.

Conclusions: NVX-CoV2373 was safe and effective for the prevention of Covid-19. Most breakthrough cases were caused by contemporary variant strains."

Emerg Infect Dis: [Effectiveness of mRNA BNT162b2 vaccine 6 months after vaccination among patients in large health maintenance organization, Israel](#) (14 December 2021)

"Israel experienced a new wave of coronavirus disease during June 2021, six months after implementing a national vaccination campaign. We conducted 3 discrete analyses using data from a large health maintenance organization in Israel to determine whether IgG levels of fully vaccinated persons decrease over time, describe the relationship between IgG titer and subsequent PCR-confirmed infection, and compare PCR-confirmed infection rates by period of vaccination. Mean IgG levels steadily decreased over the 6-month period in the total tested population and in all age groups. An inverse relationship was found between IgG titer and subsequent PCR-positive infection. Persons vaccinated during the first 2 months of the campaign were more likely to become infected than those subsequently vaccinated. The vaccinated group >60 years of age had lower initial IgG levels and were at greater risk for infection. The findings support the decision to add a booster vaccine for persons >60 years of age."

NEJM: [Waning Immunity after the BNT162b2 Vaccine in Israel](#) (09 December 2021)

"Background: In December 2020, Israel began a mass vaccination campaign against coronavirus disease 2019 (Covid-19) by administering the BNT162b2 vaccine, which led to a sharp curtailing of the outbreak. After a period with almost no cases of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, a resurgent Covid-19 outbreak began in mid-June 2021. Possible reasons for the resurgence were reduced vaccine effectiveness against the delta (B.1.617.2) variant and waning immunity. The extent of waning immunity of the vaccine against the delta variant in Israel is unclear.

Methods: We used data on confirmed infection and severe disease collected from an Israeli national database for the period of July 11 to 31, 2021, for all Israeli residents who had been fully vaccinated before June 2021. We used a Poisson regression model to compare rates of confirmed SARS-CoV-2 infection and severe Covid-19 among persons vaccinated during different time periods, with stratification according to age group and with adjustment for possible confounding factors.

Results: Among persons 60 years of age or older, the rate of infection in the July 11-31 period was higher among persons who became fully vaccinated in January 2021 (when they were first eligible) than among those fully vaccinated 2 months later, in March (rate ratio, 1.6; 95% confidence interval [CI], 1.3 to 2.0). Among persons 40 to 59 years of age, the rate ratio for infection among those fully vaccinated in February (when they were first eligible), as compared with 2 months later, in April, was 1.7 (95% CI, 1.4 to 2.1). Among persons 16 to 39 years of age, the rate ratio for infection among those fully vaccinated in March (when they were first eligible), as compared with 2 months later, in May, was 1.6 (95% CI, 1.3 to 2.0). The rate ratio for severe disease among persons fully vaccinated in the month when they were first eligible, as compared with those fully vaccinated in March, was 1.8 (95% CI, 1.1 to 2.9) among persons 60 years of age or older and 2.2 (95% CI, 0.6 to 7.7) among those

40 to 59 years of age; owing to small numbers, the rate ratio could not be calculated among persons 16 to 39 years of age.

Conclusions: These findings indicate that immunity against the delta variant of SARS-CoV-2 waned in all age groups a few months after receipt of the second dose of vaccine."

Sci Transl Med: [Robust immune responses are observed after one dose of BNT162b2 mRNA vaccine dose in SARS-CoV-2 experienced individuals](#) (07 December 2021)

"The use of COVID-19 vaccines will play the major role in helping to end the pandemic that has killed millions worldwide. COVID-19 vaccines have resulted in robust humoral responses and protective efficacy in human trials, but efficacy trials excluded individuals with a prior diagnosis of COVID-19. As a result, little is known about how immune responses induced by mRNA vaccines differ in individuals who recovered from COVID-19. Here, we evaluated longitudinal immune responses to two-dose BNT162b2 mRNA vaccination in 15 adults who had experienced COVID-19, compared to 21 adults who did not have prior COVID-19. Consistent with prior studies of mRNA vaccines, we observed robust cytotoxic CD8+ T cell responses in both cohorts following the second dose. Furthermore, SARS-CoV-2-naïve individuals had progressive increases in humoral and antigen-specific antibody-secreting cell (ASC) responses following each dose of vaccine, whereas SARS-CoV-2-experienced individuals demonstrated strong humoral and antigen-specific ASC responses to the first dose but these responses were not further enhanced after the second dose of the vaccine at the time points studied. Together, these data highlight the relevance of immunological history for understanding vaccine immune responses and may have implications for personalizing mRNA vaccination regimens used to prevent COVID-19, including for the deployment of booster shots."

### *Boosters*

MMWR: [Booster and Additional Primary Dose COVID-19 Vaccinations Among Adults Aged ≥65 Years — United States, August 13, 2021–November 19, 2021](#) (17 December 2021)

"What is already known about this topic? Although COVID-19 vaccines are highly effective, vaccine effectiveness wanes over time, and adults aged ≥65 years are at increased risk for severe COVID-19–associated illness. Booster and additional primary vaccine doses increase protection.

What is added by this report? During August 13–November 19, 2021, 18.7 million persons aged ≥65 years received a booster or additional primary dose of COVID-19 vaccine, constituting 44.1% of eligible persons aged ≥65 years. Coverage differed by primary series vaccine product and race/ethnicity.

What are the implications for public health practice? Strategic efforts are needed to encourage eligible persons aged  $\geq 18$  years, especially those aged  $\geq 65$  years and those who are immunocompromised, to receive a booster and/or additional primary dose to ensure maximal protection against COVID-19."

NEJM: [Protection against Covid-19 by BNT162b2 Booster across Age Groups](#) (08 December 2021)

"Background: After promising initial results from the administration of a third (booster) dose of the BNT162b2 messenger RNA vaccine (Pfizer-BioNTech) to persons 60 years of age or older, the booster campaign in Israel was gradually expanded to persons in younger age groups who had received a second dose at least 5 months earlier.

Methods: We extracted data for the period from July 30 to October 10, 2021, from the Israel Ministry of Health database regarding 4,696,865 persons 16 years of age or older who had received two doses of BNT162b2 at least 5 months earlier. In the primary analysis, we compared the rates of confirmed coronavirus disease 2019 (Covid-19), severe illness, and death among those who had received a booster dose at least 12 days earlier (booster group) with the rates among those who had not received a booster (nonbooster group). In a secondary analysis, we compared the rates in the booster group with the rates among those who had received a booster 3 to 7 days earlier (early postbooster group). We used Poisson regression models to estimate rate ratios after adjusting for possible confounding factors.

Results: The rate of confirmed infection was lower in the booster group than in the nonbooster group by a factor of approximately 10 (range across five age groups, 9.0 to 17.2) and was lower in the booster group than in the early postbooster group by a factor of 4.9 to 10.8. The adjusted rate difference ranged from 57.0 to 89.5 infections per 100,000 person-days in the primary analysis and from 34.4 to 38.3 in the secondary analysis. The rates of severe illness in the primary and secondary analyses were lower in the booster group by a factor of 17.9 (95% confidence interval [CI], 15.1 to 21.2) and 6.5 (95% CI, 5.1 to 8.2), respectively, among those 60 years of age or older and by a factor of 21.7 (95% CI, 10.6 to 44.2) and 3.7 (95% CI, 1.3 to 10.2) among those 40 to 59 years of age. The adjusted rate difference in the primary and secondary analyses was 5.4 and 1.9 cases of severe illness per 100,000 person-days among those 60 years of age or older and 0.6 and 0.1 among those 40 to 59 years of age. Among those 60 years of age or older, mortality was lower by a factor of 14.7 (95% CI, 10.0 to 21.4) in the primary analysis and 4.9 (95% CI, 3.1 to 7.9) in the secondary analysis. The adjusted rate difference in the primary and secondary analyses was 2.1 and 0.8 deaths per 100,000 person-days.

Conclusions: Across the age groups studied, rates of confirmed Covid-19 and severe illness were substantially lower among participants who received a booster dose of the BNT162b2 vaccine than among those who did not."

NEJM: [BNT162b2 Vaccine Booster and Mortality Due to Covid-19](#) (08 December 2021)

"Background: The emergence of the B.1.617.2 (delta) variant of severe acute respiratory syndrome coronavirus 2 and the reduced effectiveness over time of the BNT162b2 vaccine (Pfizer-BioNTech) led to a resurgence of coronavirus disease 2019 (Covid-19) cases in populations that had been vaccinated early. On July 30, 2021, the Israeli Ministry of Health approved the use of a third dose of BNT162b2 (booster) to cope with this resurgence. Evidence regarding the effectiveness of the booster in lowering mortality due to Covid-19 is still needed.

Methods: We obtained data for all members of Clalit Health Services who were 50 years of age or older at the start of the study and had received two doses of BNT162b2 at least 5 months earlier. The mortality due to Covid-19 among participants who received the booster during the study period (booster group) was compared with that among participants who did not receive the booster (nonbooster group). A Cox proportional-hazards regression model with time-dependent covariates was used to estimate the association of booster status with death due to Covid-19, with adjustment for sociodemographic factors and coexisting conditions.

Results: A total of 843,208 participants met the eligibility criteria, of whom 758,118 (90%) received the booster during the 54-day study period. Death due to Covid-19 occurred in 65 participants in the booster group (0.16 per 100,000 persons per day) and in 137 participants in the nonbooster group (2.98 per 100,000 persons per day). The adjusted hazard ratio for death due to Covid-19 in the booster group, as compared with the nonbooster group, was 0.10 (95% confidence interval, 0.07 to 0.14;  $P < 0.001$ ).

Conclusions: Participants who received a booster at least 5 months after a second dose of BNT162b2 had 90% lower mortality due to Covid-19 than participants who did not receive a booster."

JAMA: [Antibody Titers Before and After a Third Dose of the SARS-CoV-2 BNT162b2 Vaccine in Adults Aged ≥60 Years](#) (07 December 2021)

"This study assesses antispikes (anti-S) IgG antibody titers before and after a third BNT162b2 dose (booster) in individuals aged 60 years and older in Israel....

This study found that a third BNT162b2 dose in adults aged 60 years and older was associated with significantly increased IgG titers after 10 to 19 days, with no major adverse events."

## *Myocarditis*

BMJ: [SARS-CoV-2 vaccination and myocarditis or myopericarditis: population based cohort study](#) (16 December 2021)

"Objective: To investigate the association between SARS-CoV-2 vaccination and myocarditis or myopericarditis.

Main outcome measures: The primary outcome, myocarditis or myopericarditis, was defined as a combination of a hospital diagnosis of myocarditis or pericarditis, increased troponin levels, and a hospital stay lasting more than 24 hours. Follow-up time before vaccination was compared with follow-up time 0-28 days from the day of vaccination for both first and second doses, using Cox proportional hazards regression with age as an underlying timescale to estimate hazard ratios adjusted for sex, comorbidities, and other potential confounders.

Results: During follow-up, 269 participants developed myocarditis or myopericarditis, of whom 108 (40%) were 12-39 years old and 196 (73%) were male. Of 3 482 295 individuals vaccinated with BNT162b2 (Pfizer-BioNTech), 48 developed myocarditis or myopericarditis within 28 days from the vaccination date compared with unvaccinated individuals (adjusted hazard ratio 1.34 (95% confidence interval 0.90 to 2.00); absolute rate 1.4 per 100 000 vaccinated individuals within 28 days of vaccination (95% confidence interval 1.0 to 1.8)). Adjusted hazard ratios among female participants only and male participants only were 3.73 (1.82 to 7.65) and 0.82 (0.50 to 1.34), respectively, with corresponding absolute rates of 1.3 (0.8 to 1.9) and 1.5 (1.0 to 2.2) per 100 000 vaccinated individuals within 28 days of vaccination, respectively. The adjusted hazard ratio among 12-39 year olds was 1.48 (0.74 to 2.98) and the absolute rate was 1.6 (1.0 to 2.6) per 100 000 vaccinated individuals within 28 days of vaccination. Among 498 814 individuals vaccinated with mRNA-1273 (Moderna), 21 developed myocarditis or myopericarditis within 28 days from vaccination date (adjusted hazard ratio 3.92 (2.30 to 6.68); absolute rate 4.2 per 100 000 vaccinated individuals within 28 days of vaccination (2.6 to 6.4)). Adjusted hazard ratios among women only and men only were 6.33 (2.11 to 18.96) and 3.22 (1.75 to 5.93), respectively, with corresponding absolute rates of 2.0 (0.7 to 4.8) and 6.3 (3.6 to 10.2) per 100 000 vaccinated individuals within 28 days of vaccination, respectively. The adjusted hazard ratio among 12-39 year olds was 5.24 (2.47 to 11.12) and the absolute rate was 5.7 (3.3 to 9.3) per 100 000 vaccinated individuals within 28 days of vaccination.

Conclusions: Vaccination with mRNA-1273 was associated with a significantly increased risk of myocarditis or myopericarditis in the Danish population, primarily driven by an increased risk among individuals aged 12-39 years, while BNT162b2 vaccination was only associated with a significantly increased risk among women. However, the absolute rate of myocarditis or myopericarditis after SARS-CoV-2 mRNA vaccination was low, even in younger age

groups. The benefits of SARS-CoV-2 mRNA vaccination should be taken into account when interpreting these findings. Larger multinational studies are needed to further investigate the risks of myocarditis or myopericarditis after vaccination within smaller subgroups."

See also: [editorial](#)

Circulation: [Clinically Suspected Myocarditis Temporally Related to COVID-19 Vaccination in Adolescents and Young Adults](#) (06 December 2021)

"Background: Understanding the clinical course and short-term outcomes of suspected myocarditis following COVID-19 vaccination has important public health implications in the decision to vaccinate youth.

Methods: We retrospectively collected data on patients <21 years-old presenting before 7/4/2021 with suspected myocarditis within 30 days of COVID-19 vaccination. Lake Louise criteria were used for cardiac magnetic resonance imaging (cMRI) findings. Myocarditis cases were classified as confirmed or probable based on the Centers for Disease Control and Prevention definitions.

Results: We report on 139 adolescents and young adults with 140 episodes of suspected myocarditis (49 confirmed, 91 probable) at 26 centers. Most patients were male (N=126, 90.6%) and White (N=92, 66.2%); 29 (20.9%) were Hispanic; and median age was 15.8 years (range 12.1-20.3, IQR 14.5-17.0). Suspected myocarditis occurred in 136 patients (97.8%) following mRNA vaccine, with 131 (94.2%) following the Pfizer-BioNTech vaccine; 128 (91.4%) occurred after the 2nd dose. Symptoms started a median of 2 days (range 0-22, IQR 1-3) after vaccination. The most common symptom was chest pain (99.3%). Patients were treated with nonsteroidal anti-inflammatory drugs (81.3%), intravenous immunoglobulin (21.6%), glucocorticoids (21.6%), colchicine (7.9%) or no anti-inflammatory therapies (8.6%). Twenty-six patients (18.7%) were in the ICU, two were treated with inotropic/vasoactive support, and none required ECMO or died. Median hospital stay was 2 days (range 0-10, IQR 2-3). All patients had elevated troponin I (N=111, 8.12 ng/mL, IQR 3.50-15.90) or T (N=28, 0.61 ng/mL, IQR 0.25-1.30); 69.8% had abnormal electrocardiograms and/or arrhythmias (7 with non-sustained ventricular tachycardia); and 18.7% had left ventricular ejection fraction (LVEF) <55% on echocardiogram. Of 97 patients who underwent cMRI at median 5 days (range 0-88, IQR 3-17) from symptom onset, 75 (77.3%) had abnormal findings: 74 (76.3%) had late gadolinium enhancement, 54 (55.7%) had myocardial edema, and 49 (50.5%) met Lake Louise criteria. Among 26 patients with LVEF <55% on echocardiogram, all with follow-up had normalized function (N=25).

Conclusions: Most cases of suspected COVID-19 vaccine myocarditis occurring in persons <21 years have a mild clinical course with rapid resolution of symptoms. Abnormal findings on cMRI were frequent. Future studies should evaluate risk factors, mechanisms, and long-term outcomes."

## Breakthrough Infections, Reinfections, and Coinfections

### *News in Brief*

"Don't be surprised when you get omicron. America is in for a lot more breakthrough infections. Here's what to do if you fall sick" ([Atlantic](#)).

### *Journal Articles*

JAMA: [Antibody Response and Variant Cross-Neutralization After SARS-CoV-2 Breakthrough Infection](#) (16 December 2021)

"This study of fully vaccinated health care workers examines antibody levels and variant cross-neutralization after COVID-19 breakthrough infection....

Results of this study showed substantial boosting of humoral immunity after breakthrough infection, despite predominantly mild disease. Boosting was most notable for IgA, possibly due to the differences in route of exposure between vaccination and natural infection. In addition, breakthrough sera demonstrated improved variant cross-neutralization, and Delta breakthrough infections in particular exhibited improved potency against Delta vs WA1, suggesting that the protective immune response may be broadened through development of variant boosters with antigenic inserts matching the emerging SARS-CoV-2 variants."

Clin Infect Dis: [Rate and Risk Factors for Severe/Critical Disease Among Fully Vaccinated Persons with Breakthrough SARS-CoV-2 Infection in a High-risk National Population](#) (10 December 2021)

"Background: Breakthrough SARS-CoV-2 infections after vaccination have been reported. Outcomes among persons with breakthrough infection are poorly understood.

Methods: We identified all Veterans with a confirmed SARS-CoV-2 infection >14 days after the second dose of an mRNA vaccine between December 15, 2020 and June 30, 2021, and propensity-score matched unvaccinated controls with SARS-CoV-2 infection. Primary outcome was severe/critical disease, defined as admission to an intensive care unit, mechanical ventilation, or death within 28 days of diagnosis or during index hospitalization.

Results: Among 502,780 vaccinated and 599,974 unvaccinated persons, there were 2,332 (0.5%) breakthrough infections in the vaccinated group and 40,540 (6.8%) infections in the unvaccinated group over a follow up period of 69,083 person-days in each group. Among these groups, we identified 1,728 vaccinated persons with breakthrough infection (cases) and 1,728 propensity-score matched unvaccinated controls with infection. Among the former, 95 (5.5%) persons met the criteria for severe/critical disease, while 200 (11.6%) persons met the criteria among the latter group. Incidence rate for severe/critical disease per 1,000 person-days (95% CI) was 0.55 (0.45-0.68) among the former and 1.22 (1.07-1.41)

among the latter group ( $P < 0.0001$ ). Risk was higher (HR, 95% CI) with increasing age (per 10-year increase 1.25; 1.11-1.41), and those with  $>4$  comorbidities (2.85; 1.49-5.43), while being vaccinated was associated with strong protection against severe/critical disease (HR 0.41; 0.32-0.52).

Conclusion: Rate of severe/critical disease is higher among older persons and those with  $>4$  comorbidities, but lower among fully vaccinated persons with breakthrough infection compared with unvaccinated controls who develop infection."

JAMA Ophthalmol: [Cumulative Mortality and Factors Associated With Outcomes of Mucormycosis After COVID-19 at a Multispecialty Tertiary Care Center in India](#) (09 December 2021)

"Question: What is the mortality rate among patients with COVID-19–associated rhino-orbitocerebral mucormycosis at 1 month?

Findings: In this case-control study of 73 patients, 26 (36%) died within 10 days after admission. The cumulative probability of death was 53% at day 21, and assisted ventilation during prior COVID-19 treatment or visual acuity of no light perception were associated with a higher risk of death.

Meaning: These findings suggest that the mortality rate after rhino-orbitocerebral mucormycosis is high and that a subgroup of patients who have severe COVID-19 or present with severe orbital disease are more likely to die within 10 days of admission."

Emerg Infect Dis: [Comparative effectiveness of coronavirus vaccine in preventing breakthrough infections among vaccinated persons infected with Delta and Alpha variants](#) (07 December 2021)

"We developed a case–case study to compare mRNA vaccine effectiveness against Delta versus Alpha coronavirus variants. We used data on 2,097 case-patients with PCR-positive severe acute respiratory syndrome coronavirus 2 infections reported in Portugal during May–July 2021. We estimated the odds of vaccine breakthrough infection in Delta-infected versus Alpha-infected patients by using conditional logistic regression adjusted for age group and sex and matched by the week of diagnosis. We compared reverse-transcription PCR cycle threshold values by vaccination status and variant as an indirect measure of viral load. We found significantly higher odds of vaccine breakthrough infection in Delta-infected patients than in Alpha-infected patients (odds ratio 1.96 [95% CI 1.22–3.14]), suggesting lower effectiveness of the mRNA vaccines in preventing infection with the Delta variant. We estimated lower mean cycle threshold values for the Delta cases (mean difference  $-2.10$  [95% CI  $-2.74$  to  $-1.47$ ]), suggesting higher infectiousness than the Alpha variant."

## Treatments and Management

### *News in Brief*

The NIH has updated its COVID-19 treatment guidelines; [see what's new](#).

"FDA authorizes new long-acting monoclonal antibodies for pre-exposure prevention of COVID-19 in certain individuals" ([FDA](#)).

In a phase 2/3 trial, Pfizer's oral COVID-19 antiviral (nirmatrelvir-ritonavir; Paxlovid) reduced the risk of hospitalization or death by 89% if taken within 3 days of symptom onset and by 88% if taken within 5 days ([Pfizer](#)).

"Merck's COVID pill loses its lustre: what that means for the pandemic — molnupiravir was initially heralded by public-health officials as a game-changer for COVID-19, but full clinical-trial data showed lower-than-expected efficacy" ([Nature](#)).

"Regeneron and AstraZeneca give mixed results on potency of coronavirus antibody cocktails against omicron" ([WP](#)).

"As the omicron variant threatens to wipe out monoclonal antibodies, the U.S. is saving up one that will still work — sotrovimab, a treatment from Vir Biotechnology and GlaxoSmithKline, is expected to remain effective against omicron" ([WP](#)).

### *Journal Articles*

Clin Infect Dis: [Real-World Effectiveness Of Remdesivir In Adults Hospitalized With Covid-19: A Retrospective, Multicenter Comparative Effectiveness Study](#) (15 December 2021)

"Background: There is an urgent need to understand the real-world effectiveness of remdesivir in the treatment of SARS-CoV-2.

Methods: This was a retrospective comparative effectiveness study. Individuals hospitalized in a large private healthcare network in the US from February 23, 2020 through February 11, 2021 with a positive test for SARS-CoV-2 and ICD-10 diagnosis codes consistent with symptomatic COVID-19 were included. Remdesivir recipients were matched to controls using time-dependent propensity scores. The primary outcome was time to improvement with a secondary outcome of time to death.

Results: Of 96,859 COVID-19 patients, 42,473 (43.9%) received at least one remdesivir dose. The median age of remdesivir recipients was 65 years, 23,701 (55.8%) were male and 22,819 (53.7%) were non-white. Matches were found for 18,328 patients (43.2%).

Remdesivir recipients were significantly more likely to achieve clinical improvement by 28 days (adjusted hazard ratio [1.19, 95% confidence interval (CI), 1.16-1.22]). Remdesivir

patients on no oxygen (aHR 1.30, 95% CI 1.22-1.38) or low-flow oxygen (aHR 1.23, 95% CI 1.19-1.27) were significantly more likely to achieve clinical improvement by 28 days. There was no significant impact on the likelihood of mortality overall (aHR 1.02, 95% CI 0.97-1.08). Remdesivir recipients on low-flow oxygen were significantly less likely to die than controls (aHR 0.85, 95% CI 0.77-0.92; 28-day mortality 8.4% [865 deaths] for remdesivir patients, 12.5% [1,334 deaths] for controls).

Conclusions: These results support the use of remdesivir for hospitalized COVID-19 patients on no or low-flow oxygen. Routine initiation of remdesivir in more severely ill patients is unlikely to be beneficial."

JAMA Intern Med: [Efficacy and Safety of COVID-19 Convalescent Plasma in Hospitalized Patients: A Randomized Clinical Trial](#) (13 December 2021)

"Question: Does COVID-19 convalescent plasma (CCP), compared with placebo, improve the clinical status of hospitalized patients with COVID-19 requiring noninvasive supplemental oxygen?

Findings: In this randomized clinical trial including 941 patients, based on the World Health Organization 11-point Ordinal Scale for Clinical Improvement, CCP did not benefit 468 participants randomized to CCP compared with 473 randomized to placebo from April 2020 to March 2021. However, in exploratory analyses, CCP appeared to benefit those enrolled from April to June 2020, the period when most participants received high-titer CCP and were not receiving remdesivir and corticosteroids at randomization.

Meaning: In this trial, CCP did not meet prespecified outcomes for efficacy, but high-titer CCP may have benefited hospitalized patients with COVID-19 early in the pandemic when other treatments were not in use, suggesting a heterogenous treatment effect over time."

Clin Infect Dis: [Circulating ubiquitous RNA, a highly predictive and prognostic biomarker in hospitalized COVID-19 patients](#) (11 December 2021)

"Background: Approximately 15-30% of hospitalized COVID-19 patients develop acute respiratory distress syndrome, systemic tissue injury, and/or multi-organ failure leading to death in around 45% of cases. There is a clear need for biomarkers which quantify tissue injury, predict clinical outcomes and guide the clinical management of hospitalized COVID-19 patients.

Methods: We herein report the quantification by droplet-based digital PCR (ddPCR) of the SARS-CoV-2 RNAemia and the plasmatic release of a ubiquitous human intracellular marker, the ribonuclease P (RNase P) in order to evaluate tissue injury and cell lysis in the plasma of 139 COVID-19 hospitalized patients at admission.

Results: We confirmed that SARS-CoV-2 RNAemia was associated with clinical severity of COVID-19 patients. In addition, we showed that plasmatic RNase P RNAemia at admission was also highly correlated with disease severity ( $P < 0.001$ ) and invasive mechanical ventilation status ( $P < 0.001$ ) but not with pulmonary severity. Altogether, these results indicate a consequent cell lysis process in severe and critical patients but not systematically due to lung cell death. Finally, the plasmatic RNase P RNA value was also significantly associated with overall survival.

Conclusion: Viral and ubiquitous blood biomarkers monitored by ddPCR could be useful for the clinical monitoring and the management of hospitalized COVID-19 patients. Moreover, these results could pave the way for new and more personalized circulating biomarkers in COVID-19, and more generally in infectious diseases, specific from each patient organ injury profile."

JAMA Netw Open: [Adherence of Clinical Practice Guidelines for Pharmacologic Treatments of Hospitalized Patients With COVID-19 to Trustworthy Standards: A Systematic Review](#) (10 December 2021)

"Question: Do clinical practice guidelines (CPGs) that report on pharmacologic treatments of hospitalized patients with COVID-19 meet the National Academy of Medicine standards for trustworthiness?

Findings: In this systematic review of 32 CPGs of predominantly low quality, few reported funding sources or conflicts of interest, included a methodologist, described a search strategy or study selection process, or synthesized evidence. Although 14 CPGs (43.8%) made recommendations or suggestions for or against treatments, they infrequently rated the confidence in the quality of the evidence (6 [18.8%]), described potential benefits and harms (6 [18.8%]), or graded the strength of recommendations (5 [15.6%]).

Meaning: The findings of this study suggest that few COVID-19 CPGs meet National Academy of Medicine standards for trustworthy guidelines."

JAMA Netw Open: [Trends in US Surgical Procedures and Health Care System Response to Policies Curtailing Elective Surgical Operations During the COVID-19 Pandemic](#) (08 December 2021)

"Question: Were 2 separate COVID-19 crises, one policy driven during the initial shutdown and the other occurring during the highest burden of infections, associated with changes in surgical procedure volume in the US surgical health system?

Findings: In this cohort study of more than 13 million US surgical procedures from January 1, 2019, through January 30, 2021, there was a 48.0% decrease in total surgical procedure volume immediately after the March 2020 recommendation to cancel elective surgical

procedures. Surgical volume returned to 2019 rates in all surgical specialties except otolaryngology, a rate maintained during the COVID-19 peak surge in fall and winter.

Meaning: These findings suggest that health systems learned to adapt and were able to self-regulate, maintaining surgical procedure volume during the largest peak in volume of patients with COVID-19."

JAMA: [Effect of High-Flow Oxygen Therapy vs Conventional Oxygen Therapy on Invasive Mechanical Ventilation and Clinical Recovery in Patients With Severe COVID-19: A Randomized Clinical Trial](#) (07 December 2021)

"Question: Does the use of high-flow oxygen therapy through a nasal cannula, compared with conventional oxygen therapy, reduce requirement of intubation and time to clinical improvement among patients with severe COVID-19?

Findings: In this randomized clinical trial that included 220 patients with severe COVID-19, the rate of intubation and mechanical ventilation for those treated with high-flow oxygen therapy through a nasal cannula vs with conventional oxygen therapy was 34.3% vs 51.0%, respectively; the median time to clinical recovery was 11 days vs 14 days. Both comparisons were statistically significant.

Meaning: Among patients with severe COVID-19, treatment with high-flow oxygen therapy compared with conventional oxygen therapy reduced the likelihood of invasive mechanical ventilation and decreased time to clinical recovery."

## **Pre-Existing Conditions, Comorbidities, and Impact on Other Health Issues**

### ***News in Brief***

"Surge in Americans skipping medical care due to cost, Gallup says" ([CBS](#)).

### ***Journal Articles***

JAMA Cardiol: [Association of Complement and MAPK Activation With SARS-CoV-2–Associated Myocardial Inflammation](#) (15 December 2021)

"Question: What is the cardiac phenotype of patients with SARS-CoV-2 infection compared with viral and immune-mediated myocarditis and noninflammatory cardiomyopathy?

Findings: In this case series of 19 patients undergoing endomyocardial biopsies, cardiac specimens of patients with SARS-CoV-2 infection had a higher abundance of complement-

associated factors and serine/threonine protein kinases, with mitogen-activated protein kinase-associated pathways having the highest abundance. Similarities in the cardiac immune signature were found among those with SARS-CoV-2 infection and viral myocarditis.

Meaning: In this study, the exploratory data, which characterized myocardial inflammation by deep phenotyping, have implications for the development of treatment strategies to reduce SARS-CoV-2-mediated tissue injury; these findings require confirmation in a prospective and extended cohort of patients."

Nat Med: [Risks of myocarditis, pericarditis, and cardiac arrhythmias associated with COVID-19 vaccination or SARS-CoV-2 infection](#) (14 December 2021)

"Although myocarditis and pericarditis were not observed as adverse events in coronavirus disease 2019 (COVID-19) vaccine trials, there have been numerous reports of suspected cases following vaccination in the general population. We undertook a self-controlled case series study of people aged 16 or older vaccinated for COVID-19 in England between 1 December 2020 and 24 August 2021 to investigate hospital admission or death from myocarditis, pericarditis and cardiac arrhythmias in the 1–28 days following adenovirus (ChAdOx1, n = 20,615,911) or messenger RNA-based (BNT162b2, n = 16,993,389; mRNA-1273, n = 1,006,191) vaccines or a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) positive test (n = 3,028,867). We found increased risks of myocarditis associated with the first dose of ChAdOx1 and BNT162b2 vaccines and the first and second doses of the mRNA-1273 vaccine over the 1–28 days postvaccination period, and after a SARS-CoV-2 positive test. We estimated an extra two (95% confidence interval (CI) 0, 3), one (95% CI 0, 2) and six (95% CI 2, 8) myocarditis events per 1 million people vaccinated with ChAdOx1, BNT162b2 and mRNA-1273, respectively, in the 28 days following a first dose and an extra ten (95% CI 7, 11) myocarditis events per 1 million vaccinated in the 28 days after a second dose of mRNA-1273. This compares with an extra 40 (95% CI 38, 41) myocarditis events per 1 million patients in the 28 days following a SARS-CoV-2 positive test. We also observed increased risks of pericarditis and cardiac arrhythmias following a positive SARS-CoV-2 test. Similar associations were not observed with any of the COVID-19 vaccines, apart from an increased risk of arrhythmia following a second dose of mRNA-1273. Subgroup analyses by age showed the increased risk of myocarditis associated with the two mRNA vaccines was present only in those younger than 40."

Clin Infect Dis: [Hyperinflammatory syndromes after SARS-CoV-2 mRNA vaccination in individuals with underlying immune dysregulation](#) (10 December 2021)

"The development of effective SARS-CoV-2 mRNA vaccines has been a significant accomplishment. Adverse events are extremely rare, but continued surveillance is important, especially in at-risk populations. In 5-patients with preexisting immune

dysregulation, hyperinflammatory syndromes, including hemophagocytic lymphohistiocytosis, developed after SARS-CoV-2 mRNA vaccination. Early recognition of this rare condition is essential."

Cancer: [Impact of the COVID-19 pandemic on diagnosis of new cancers: A national multicenter study of the Veterans Affairs Healthcare System](#) (06 December 2021)

"Background: The coronavirus disease 2019 (COVID-19) pandemic caused disruptions in treatment for cancer. Less is known about its impact on new cancer diagnoses, where delays could cause worsening long-term outcomes. This study quantifies decreases in encounters related to prostate, lung, bladder and colorectal cancers, procedures that facilitate their diagnosis, and new diagnoses of those cancers in the COVID era compared to pre-COVID era.

Methods: All encounters at Veterans' Affairs facilities nationwide from 2016 through 2020 were reviewed. The authors quantified trends in new diagnoses of cancer and in procedures facilitating their diagnosis, from January 1, 2018 onward. Using 2018 to 2019 as baseline, reductions in procedures and new cancer diagnoses in 2020 were estimated. Calculated absolute and percentage differences in annual volume and observed-to-expected volume ratios were calculated. Heat maps and funnel plots of volume changes were generated.

Results: From 2018 through 2020, there were 4.1 million cancer-related encounters, 3.9 million relevant procedures, and 251,647 new cancers diagnosed. Compared to the annual averages in 2018 through 2019, colonoscopies in 2020 decreased by 45% whereas prostate biopsies, chest computed tomography scans, and cystoscopies decreased by 29%, 10%, and 21%, respectively. New cancer diagnoses decreased by 13% to 23%. These drops varied by state and continued to accumulate despite reductions in pandemic-related restrictions.

Conclusion: The authors identified substantial reductions in procedures used to diagnose cancer and subsequent reductions in new diagnoses of cancer across the United States because of the COVID-19 pandemic. A nomogram is provided to identify and resolve these unmet health care needs and avoid worse long-term cancer outcomes."

Front Cardiovasc Med: [Heart Failure Probability and Early Outcomes of Critically Ill Patients With COVID-19: A Prospective, Multicenter Study](#) (26 November 2021)

"Background: The relationship between cardiac functions and the fatal outcome of coronavirus disease 2019 (COVID-19) is still largely underestimated. We aim to explore the role of heart failure (HF) and NT-proBNP in the prognosis of critically ill patients with COVID-19 and construct an easy-to-use predictive model using machine learning.

Methods: In this multicenter and prospective study, a total of 1,050 patients with clinical suspicion of COVID-19 were consecutively screened. Finally, 402 laboratory-confirmed critically ill patients with COVID-19 were enrolled. A "triple cut-point" strategy of NT-

proBNP was applied to assess the probability of HF. The primary outcome was 30-day all-cause in-hospital death. Prognostic risk factors were analyzed using the least absolute shrinkage and selection operator (LASSO) and multivariate logistic regression, further formulating a nomogram to predict mortality.

Results: Within a 30-day follow-up, 27.4% of the 402 patients died. The mortality rate of patients with HF likely was significantly higher than that of the patient with gray zone and HF unlikely (40.8% vs. 25 and 16.5%, respectively,  $P < 0.001$ ). HF likely [Odds ratio (OR) 1.97, 95% CI 1.13-3.42], age (OR 1.04, 95% CI 1.02-1.06), lymphocyte (OR 0.36, 95% CI 0.19-0.68), albumin (OR 0.92, 95% CI 0.87-0.96), and total bilirubin (OR 1.02, 95% CI 1-1.04) were independently associated with the prognosis of critically ill patients with COVID-19. Moreover, a nomogram was developed by bootstrap validation, and C-index was 0.8 (95% CI 0.74-0.86).

Conclusions: This study established a novel nomogram to predict the 30-day all-cause mortality of critically ill patients with COVID-19, highlighting the predominant role of the "triple cut-point" strategy of NT-proBNP, which could assist in risk stratification and improve clinical sequelae."

## Long COVID / Post-COVID Period

### *News in Brief*

"Long COVID guidance focuses on breathing discomfort, cognitive symptoms — psychiatry society builds on previous guidance on fatigue" ([Medscape](#); see also: [full text in PM&R](#)).

Listen: "Vaccines and long COVID, how protected are you?" ([Coronapod](#))

Long read: "Long covid is destroying careers, leaving economic distress in its wake — Suffering from debilitating exhaustion and pain for months, patients find themselves on food stamps and Medicaid" ([WP](#)).

### *Journal Articles*

J Clin Nurs: [Symptoms and management of long COVID: A scoping review](#) (15 December 2021)

"Aim: This scoping review aims to describe published work on the symptoms and management of long COVID conditions.

Background: Symptoms and management of COVID-19 have focused on the acute stage. However, long-term consequences have also been observed.

**Methods:** A scoping review was performed based on the framework suggested by Arksey and O'Malley. We conducted a literature search to retrieve articles published from May 2020 to March 2021 in CINAHL, Cochrane library, Embase, PubMed and Web of science, including backward and forward citation tracking from the included articles. Among the 1880 articles retrieved, 34 articles met our criteria for review: 21 were related to symptom presentation and 13 to the management of long COVID.

**Results:** Long COVID symptoms were described in 21 articles. Following COVID-19 treatment, hospitalised patients most frequently reported dyspnoea, followed by anosmia/ageusia, fatigue and cough, while non-hospitalised patients commonly reported cough, followed by fever and myalgia/arthritis. Thirteen studies described management for long COVID: Focused on a multidisciplinary approach in seven articles, pulmonary rehabilitation in three articles, fatigue management in two articles and psychological therapy in one study.

**Conclusion:** People experience varied COVID-19 symptoms after treatment. However, guidelines on evidence-based, multidisciplinary management for long COVID conditions are limited in the literature. The COVID-19 pandemic may extend due to virus mutations; therefore, it is crucial to develop and disseminate evidence-based, multidisciplinary management guidelines."

Eur J Intern Med: [Factors associated with persistence of symptoms 1 year after COVID-19: A longitudinal, prospective phone-based interview follow-up cohort study](#) (07 December 2021)

**"Objective:** To investigate the persistence of symptoms compatible with COVID-19 in a real-file prospective cohort of patients at 12 months from hospital discharge.

**Methods:** Longitudinal, prospective, single-center, cohort telephone follow-up (FU) study in a Tertiary Care Hospital. All consecutive patients >18 years admitted for COVID-19 were prospectively enrolled in a telephone FU program aimed at monitoring symptoms after 1,3,6,9 and 12 months from hospital discharge. The survey screened for somatic (fatigue, dyspnea, dyspnea, palpitations, cough, chest pain, abdominal pain, ageusia, anosmia, bowel symptoms) and emotional symptoms (insomnia, confusion, altered sense of reality, loss of appetite, fear, and depression) and frailty. Only patients with 12 months FU data were analyzed (N=254). Prevalence and factors associated with symptoms were the main outcomes. Frailty was defined by the presence of  $\geq 3$  indicators: weakness, slowness/impaired mobility, weight-loss, low physical activity, and exhaustion.

**Results:** At 12 months, 40.5% of patients reported at least one symptom. The most common somatic ones were fatigue, exertional dyspnea, cough, bowel complaints while the most common psycho-emotional were insomnia, confusion, fear, and depression. Age, gender, gender, frailty, multiple symptoms at baseline and chronic obstructive pulmonary disease (COPD) were associated with symptoms persistence. Furthermore, frailty, COPD and

multiple symptoms at baseline were associated with increased risk of somatic symptoms at 12 months, while age and gender were associated with emotional ones.

Conclusions: Burden of the long COVID-19 symptoms decreased over time but remained as high as 40% at 12 months with important gender and functional differences, highlighting potential patient categories who may benefit from specific follow up strategies."

Soc Sci Med: [The contested meaning of "long COVID" - Patients, doctors, and the politics of subjective evidence](#) (30 November 2021)

"In our article, we reconstruct how the patient-made term "long COVID" was able to become a widely accepted concept in public discourses. While the condition was initially invisible to the public eye, we show how the mobilization of subjective evidence online, i.e., the dissemination of reports on the different experiences of lasting symptoms, was able to transform the condition into a crucial feature of the coronavirus pandemic.

We explore how stakeholders used the term "long COVID" in online media and in other channels to create their illness and group identity, but also to demarcate the personal experience and experiential knowledge of long COVID from that of other sources.

Our exploratory study addresses two questions. Firstly, how the mobilization of subjective evidence leads to the recognition of long COVID and the development of treatment interventions in medicine; and secondly, what distinguishes these developments from other examples of subjective evidence mobilization.

We argue that the long COVID movement was able to fill crucial knowledge gaps in the pandemic discourses, making long COVID a legitimate concern of official measures to counter the pandemic. By first showing how illness experiences were gathered that defied official classifications of COVID-19, we show how patients made the "long COVID" term. Then we compare the clinical and social identity of long COVID to that of chronic fatigue syndrome (ME/CFS), before we examine the social and epistemic processes at work in the digital and medial discourses that have transformed how the pandemic is perceived through the lens of long COVID.

Building on this, we finally demonstrate how the alignment of medical professionals as patients with the movement has challenged the normative role of clinical evidence, leading to new forms of medical action to tackle the pandemic."

## **Pediatric Population**

### ***News in Brief***

"FDA expands authorization of two monoclonal antibodies for treatment and post-exposure prevention of COVID-19 to younger pediatric patients, including newborns" ([FDA](#)).

"Pfizer files for full FDA approval of COVID-19 vaccine in adolescents" ([Reuters](#)).

"U.S. campaign to vaccinate young children off to sluggish start despite abundant supply" ([Reuters](#)).

"The U.S. surgeon general issues a stark warning about the state of youth mental health" ([NPR](#)).

### ***Journal Articles***

JAMA Netw Open: [Estimation of the Timing and Intensity of Reemergence of Respiratory Syncytial Virus Following the COVID-19 Pandemic in the US](#) (16 December 2021)

"Question: What are the factors associated with the timing and intensity of reemergent respiratory syncytial virus (RSV) epidemics following the COVID-19 pandemic?

Findings: In this simulation modeling study of a simulated population of 19.45 million people, virus introduction from external sources was associated with the spring and summer epidemics in 2021. Reemergent RSV epidemics in 2021 and 2022 were projected to be more intense and to affect patients in a broader age range than in typical RSV seasons.

Meaning: These findings suggest that the timing and intensity of reemergent RSV epidemics might be different from the usual RSV season, depending on the duration of mitigation measures and the extent of virus introduction from other regions."

JAMA Pediatr: [Association of Changes in Obesity Prevalence With the COVID-19 Pandemic in Youth in Massachusetts](#) (13 December 2021)

"This cohort study assessed obesity prevalence before and during the COVID-19 pandemic (2018-2020) in children and adolescents in Massachusetts."

Pediatrics: [Birth Hospital Length of Stay and Rehospitalization During COVID-19](#) (10 December 2021)

"Objectives: To determine if birth hospitalization length of stay (LOS) and infant rehospitalization changed during the coronavirus disease 2019 (COVID-19) era among healthy, term infants.

Methods: Retrospective cohort study using Epic's Cosmos data from 35 health systems of term infants discharged  $\leq 5$  days of birth. Short birth hospitalization LOS (vaginal birth  $< 2$

midnights; cesarean birth <3 midnights) and, secondarily, infant rehospitalization  $\leq 7$  days after birth hospitalization discharge were compared between the COVID-19 (March 1 to August 31, 2020) and prepandemic eras (March 1 to August 31, 2017, 2018, 2019). Mixed-effects models were used to estimate adjusted odds ratios (aORs) comparing the eras.

Results: Among 202 385 infants (57 110 from the COVID-19 era), short birth hospitalization LOS increased from 28.5% to 43.0% for all births (vaginal: 25.6% to 39.3%, cesarean: 40.1% to 61.0%) during the pandemic and persisted after multivariable adjustment (all: aOR 2.30, 95% confidence interval [CI] 2.25-2.36; vaginal: aOR 2.12, 95% CI 2.06-2.18; cesarean: aOR 3.01, 95% CI 2.87-3.15). Despite shorter LOS, infant rehospitalizations decreased slightly during the pandemic (1.2% to 1.1%); results were similar in adjusted analysis (all: aOR 0.83, 95% CI 0.76-0.92; vaginal: aOR 0.82, 95% CI 0.74-0.91; cesarean: aOR 0.87, 95% CI 0.69-1.10). There was no change in the proportion of rehospitalization diagnoses between eras.

Conclusions: Short infant LOS was 51% more common in the COVID-19 era, yet infant rehospitalization within a week did not increase. This natural experiment suggests shorter birth hospitalization LOS among family- and clinician-selected, healthy term infants may be safe with respect to infant rehospitalization, although examination of additional outcomes is needed."

Clin Infect Dis: [Multisystem Inflammatory Syndrome in Children—United States, February 2020–July 2021](#) (05 December 2021)

"Background: Multisystem inflammatory syndrome in children (MIS-C) is a severe hyperinflammatory condition in persons aged <21 years associated with antecedent SARS-CoV-2 infection. Our objective was to describe MIS-C cases reported to CDC's national surveillance since the COVID-19 pandemic began.

Methods: We included patients meeting the MIS-C case definition with onset date from February 19, 2020 through July 31, 2021, using CDC's MIS-C case report form, which collects information on demographics, clinical presentation, and laboratory results. Trends over time across 3 MIS-C pandemic waves were assessed using Cochran-Armitage test for categorical and Jonckheere-Terpstra test for continuous variables.

Results: Of 4,901 reported cases, 4,470 met inclusion criteria. Median patient age increased over time ( $P<0.001$ ), with a median of 9 years (interquartile range, 5-13 years) during the most recent (third) wave. Male predominance also increased (62% in third wave,  $P<0.001$ ). A significant ( $P<0.001$ ) increase in severe hematologic and gastrointestinal involvement was observed across the study period. Frequency of several cardiovascular complications (i.e., cardiac dysfunction, myocarditis, and shock/ vasopressor receipt) and renal failure declined ( $P<0.001$ ). Provision of critical care including mechanical ventilation ( $P<0.001$ ) and extracorporeal membrane oxygenation (ECMO;  $P=0.046$ ) decreased, as did duration of hospitalization and mortality (each  $P<0.001$ ).

Conclusions: Over the first 3 pandemic waves of MIS-C in the United States, cardiovascular complications and clinical outcomes including length of hospitalization, receipt of ECMO, and death decreased over time. These data serve as a baseline for monitoring future trends associated with SARS-CoV-2 B.1.617.2 (Delta) or other variants and increased COVID-19 vaccination among children."

## **Mental Health, Psychosocial Issues, and Wellness**

### ***News in Brief***

"I'm starting to give up on post-pandemic life — despair is not a mild symptom" ([Atlantic](#)).

"Finding mental-health clarity under pandemic pressures: For two decades, mycologist Matt Kasson's hyperactivity and anxiety felt like a superpower. Then COVID struck" ([Nature](#)).

Listen: "How has COVID impacted mental health?" ([Coronapod](#))

### ***Journal Articles***

Psychiatry Res: [The psychopathological impact of the SARS-CoV-2 epidemic on subjects suffering from different mental disorders: An observational retrospective study](#) (07 December 2021)

"SARS-CoV-2 infection causes a pulmonary disease (COVID-19) which spread worldwide generating fear, anxiety, depression in the general population as well as among subjects affected by mental disorders. Little is known about which different psychopathological changes the pandemic caused among individuals affected by different psychiatric disorders, which represents the aim of the present study. Specific psychometric scales were administered at three time points: T0 as outbreak of pandemic, T1 as lockdown period, T2 as reopening. Descriptive analyses and linear regression models were performed. A total of 166 outpatients were included. Overall, psychometric scores showed a significant worsening at T1 with a mild improvement at T2. Only psychopathology in schizophrenia (SKZ) patients and obsessive-compulsive (OC) symptoms did not significantly improve at T2. Subjects affected by personality disorders (PDs) resulted to be more compromised in terms of general psychopathology than depressed and anxiety/OC ones, and showed more severe anxiety symptoms than SKZ patients. In conclusion, subjects affected by PDs require specific clinical attention during COVID-19 pandemic. Moreover, the worsening of SKZ and OC symptoms should be strictly monitored by clinicians, as these aspects did not improve with

the end of lockdown measures. Further studies on larger samples are needed to confirm our results."

J Gerontol B Psychol Sci Soc Sci: [Experiencing and Forecasting COVID-19 Daily Stress on Mental Health Reactivity Across Age and Race](#) (05 December 2021)

"Objectives: This study systematically evaluates age and race differences in mental health symptoms as they unfold microlongitudinally during the coronavirus disease 2019 (COVID-19) pandemic with a focus on within-person reactivity to forecasting and experiencing COVID-19 stress.

Method: A daily diary approach was used to examine predictors of daily anxiety and depressive symptoms among 526 adults (White [54%] and Black American [46%]) aged 21-79. A total of 3,605 online diaries were collected for 21 consecutive days between October and November, 2020. In addition to mental health symptoms, participants reported forecasted (next 24 h) stress as well as experienced (past 24 h) stress related to COVID-19.

Results: Patterns of reactivity to forecasted and experienced COVID-19 stress depended on age and race. White older adults displayed greater reactivity to COVID-19-related stress than White younger adults, but the effects of COVID-19-related stress were consistently detrimental for the daily anxiety of Black Americans, regardless of age. For Black Americans, age was less negatively associated with depressive symptoms than for White Americans. Increases in experienced COVID-19 stress were also more strongly associated with increases in depressive symptoms for Black Americans relative to White participants.

Discussion: This study moves beyond cross-sectional, descriptive work within the context of the COVID-19 pandemic and emphasizes the dynamic nature of within-person reactivity patterns that differ by age and race. Although White older adults experienced an increase in daily anxiety when forecasting COVID-19 stress, the co-occurring pandemic of systemic racism may be more powerful than age-related vulnerabilities for Black adults."

## **Risk, Transmission, Exposure, and Testing**

### ***News in Brief***

"Japan researchers use ostrich cells to make glowing COVID-19 detection masks" ([Reuters](#)).

Long read: "The government asked us not to release records from the CDC's first failed COVID test. Here They Are. Federal investigation records obtained by BuzzFeed News show how one of the most pivotal mistakes of the pandemic fell on an overburdened CDC lab with only three full-time employees" ([BuzzFeed News](#); see also: [PLoS One article on CDC test](#)).

## ***Journal Articles***

JAMA Netw Open: [Global Percentage of Asymptomatic SARS-CoV-2 Infections Among the Tested Population and Individuals With Confirmed COVID-19 Diagnosis: A Systematic Review and Meta-analysis](#) (14 December 2021)

"Question: What is the percentage of asymptomatic individuals with positive test results for SARS-CoV-2 among tested individuals and those with confirmed COVID-19 diagnosis?

Findings: In this systematic review and meta-analysis of 95 unique studies with 29 776 306 individuals undergoing testing, the pooled percentage of asymptomatic infections was 0.25% among the tested population and 40.50% among the population with confirmed COVID-19.

Meaning: The high percentage of asymptomatic infections from this study highlights the potential transmission risk of asymptomatic infections in communities."

MMWR: [Community-Based Testing Sites for SARS-CoV-2 — United States, March 2020–November 2021](#) (10 December 2021)

"What is already known about this topic? Strong partnerships enable rapid, coordinated responses that support underresourced communities during public health emergencies.

What is added by this report? During March 19, 2020–April 11, 2021, the Community-Based Testing Sites (CBTS) program conducted 11,661,923 SARS-CoV-2 tests at 8,319 locations across the United States and its territories, including 3% administered through Drive-Through Testing, 87% through Pharmacies+ Testing, and 10% through Surge Testing.

What are the implications for public health practice? The CBTS program demonstrated the value of successful partnerships and collaboration for providing testing services that are responsive to local community needs. These lessons can guide current community-based screening, surveillance, and disease control programs and responses to future public health emergencies."

JAMA Netw Open: [Assessment of a Multifaceted Approach, Including Frequent PCR Testing, to Mitigation of COVID-19 Transmission at a Residential Historically Black University](#) (13 December 2021)

"Question: Would a multimodal strategy of mitigation and testing be adequate to safely reopen a residential historically Black college and university (HBCU) campus in the setting of increasing COVID-19 positivity rates?

Findings: In this cohort study among 2320 individuals at a publicly funded HBCU, combining an active messaging campaign on shared responsibility and mitigation measures with frequent polymerase chain reaction testing was associated with decreased COVID-19

positivity rates compared with the surrounding community. The need for isolation and quarantine dormitory occupancy was limited.

Meaning: This study found that, in the setting of increased community COVID-19 positivity rates and the absence of a vaccine, well-described mitigation efforts and frequent testing were associated with decreased spread of disease."

BMC Public Health: [Epidemiological features of COVID-19 patients with prolonged incubation period and its implications for controlling the epidemics in China](#) (09 December 2021)

"Background: COVID-19 patients with long incubation period were reported in clinical practice and tracing of close contacts, but their epidemiological or clinical features remained vague.

Methods: We analyzed 11,425 COVID-19 cases reported between January-August, 2020 in China. The accelerated failure time model, Logistic and modified Poisson regression models were used to investigate the determinants of prolonged incubation period, as well as their association with clinical severity and transmissibility, respectively.

Result: Among local cases, 268 (10.2%) had a prolonged incubation period of > 14 days, which was more frequently seen among elderly patients, those residing in South China, with disease onset after Level I response measures administration, or being exposed in public places. Patients with prolonged incubation period had lower risk of severe illness (OR<sub>adjusted</sub> = 0.386, 95% CI: 0.203-0.677). A reduced transmissibility was observed for the primary patients with prolonged incubation period (50.4, 95% CI: 32.3-78.6%) than those with an incubation period of ≤14 days.

Conclusions: The study provides evidence supporting a prolonged incubation period that exceeded 2 weeks in over 10% for COVID-19. Longer monitoring periods than 14 days for quarantine or persons potentially exposed to SARS-CoV-2 should be justified in extreme cases, especially for those elderly."

### *Environmental Impact of PPE*

Nat Sustain: [Increased personal protective equipment litter as a result of COVID-19 measures](#) (09 December 2021)

"Use of personal protective equipment (PPE) increased during the COVID-19 pandemic to reduce virus transmission. Here, we quantitatively analyse emergence of PPE and COVID-19-related litter over 14 months for 11 countries using the litter collection application Litterati. The proportion of masks in litter increased by >80-fold as a result of COVID-19 legislation, from <0.01% to >0.8%. Gloves and wipes, more prevalent at ~0.2% of litter before the pandemic, doubled to 0.4%, but this has since fallen. Glove litter increased in the initial

stages of the pandemic but fell after the introduction of facemask policies, whereupon there was an increase of facemask litter. National COVID-19 policy responses and international World Health Organization announcements and recommendations are a probable driver of PPE litter dynamics, especially the implementation of facemask policies. Waste management should be incorporated in designing future pandemic policies to avoid negative environmental legacies of mismanaged PPE."

Adv Sustain Syst: [Environmental Impacts of Personal Protective Clothing Used to Combat COVID- 19](#) (13 October 2021)

"Personal protective clothing is critical to shield users from highly infectious diseases including COVID-19. Such clothing is predominantly single-use, made of plastic-based synthetic fibers such as polypropylene and polyester, low cost and able to provide protection against pathogens. However, the environmental impacts of synthetic fiber-based clothing are significant and well-documented. Despite growing environmental concerns with single-use plastic-based protective clothing, the recent COVID-19 pandemic has seen a significant increase in their use, which could result in a further surge of oceanic plastic pollution, adding to the mass of plastic waste that already threatens marine life. In this review, the nature of the raw materials involved in the production of such clothing, as well as manufacturing techniques and the personal protective equipment supply chain are briefly discussed. The environmental impacts at critical points in the protective clothing value chain are identified from production to consumption, focusing on water use, chemical pollution, CO2 emissions, and waste. On the basis of these environmental impacts, the need for fundamental changes in the business model is outlined, including increased usage of reusable protective clothing, addressing supply chain "bottlenecks", establishing better waste management, and the use of sustainable materials and processes without associated environmental problems."

## **Misinformation and Health Messaging**

### ***News in Brief***

Commentary: "8 things US pandemic communicators still get wrong" ([CIDRAP](#)).

"Some doctors spreading coronavirus misinformation are being punished" ([WP](#)).

### ***Special Reports and Other Resources***

CEPA: [Jabbed in the Back: Mapping Russian and Chinese Information Operations During COVID-19](#) (02 December 2021)

"The public health and economic catastrophe of the COVID-19 pandemic has also become a battle about the nature of truth itself. From the emergence of the first reports of a virus in Wuhan, China, in December 2019, opportunistic leaders in China, Russia, and elsewhere have used the virus as an excuse to further erode democracy and wage information warfare.

They have inundated an already polluted information environment with disinformation and propaganda about the virus's origins and cures, and, most recently, vaccines. Russia largely followed its preexisting playbook of using crises to inflame tensions in foreign societies. China borrowed some tools from Russia but used them for different ends, sanitizing its own record and spreading conspiracy theories on a global scale. Little evidence suggests explicit cooperation despite some instances of narrative overlap and circular amplification between the two actors. Significant differences remain in Beijing's and Moscow's strategies and tactics in the information environment.

- During the COVID-19 pandemic, the Chinese Communist Party (CCP) spread disinformation about the efficacy of vaccines and the virus's origins, a shift from Beijing's previous disinformation campaigns, which had a narrower focus on China-specific issues such as Tibet, Hong Kong, and Taiwan.
- Most of Beijing's COVID-19 narratives aimed at shaping perceptions of China's response to the pandemic and only rarely targeted other countries specifically.
- Russia recycled previous narratives and exacerbated tensions in Western society while attempting some propaganda about Russian scientific prowess.
- The Kremlin and the CCP learned from each other. While limited evidence exists of explicit cooperation, instances of narrative overlap and circular amplification of disinformation show that China is following a Russian playbook with Chinese characteristics. Russia is simultaneously learning from the Chinese approach.
- The largest difference between China's and Russia's information warfare tactics remains China's insistence on narrative consistency, compared with Russia's firehose of falsehoods strategy. Even with substantially greater resources, this largely prevents Chinese narratives from swaying public opinion or polarizing societies.
- The two authoritarian countries' information operations have evolved over the last 18 months and will continue to do so with the spread of variants, vaccines, and inquiries into the virus's origins."

## ***Journal Articles***

Cell: [Infodemics: A new challenge for public health](#) (09 December 2021)

"The COVID-19 information epidemic, or "infodemic," demonstrates how unlimited access to information may confuse and influence behaviors during a health emergency. However, the study of infodemics is relatively new, and little is known about their relationship with epidemics management. Here, we discuss unresolved issues and propose research directions to enhance preparedness for future health crises."

BMJ Open Sci: [Misinformation: an empirical study with scientists and communicators during the COVID-19 pandemic](#) (01 December 2021)

"Objectives: To study the experiences and views within the health science community regarding the spread and prevention of science misinformation within and beyond the setting of the COVID-19 pandemic.

Methods: An exploratory study with an empirical ethics approach using qualitative interviews with Australians who produce, communicate and study health science research.

Results: Key elements that participants considered might facilitate misinformation included: the production of low-quality, fraudulent or biased science research; inadequate public access to high-quality research; insufficient public reading of high-quality research. Strategies to reduce or prevent misinformation could come from within the academic community, academic and lay media publishing systems, government funders and educators of the general public. Recommended solutions from within the scientific community included: rewarding research translation, encouraging standardised study design, increasing use of automated quality assessment tools, mandating study protocol registration, transparent peer review, facilitating wider use of open access and use of newer technologies to target public audiences. There was disagreement over whether preprints were part of the problem or part of the solution.

Conclusions: There is concern from within the health science community about systemic failings that might facilitate the production and spread of false or misleading science information. We advocate for further research into ways to minimise the production and spread of misinformation about COVID-19 and other science crises in the future."

## **Other Infectious Diseases and Public Health Issues**

### ***News in Brief***

"mRNA vaccines offer hope for HIV" ([Nat Med](#)).

"Monkeypox outbreak declared in Maniema, DRC" ([ONT](#)).

The latest Ebola outbreak in the DRC has been declared over ([WHO](#)).

"The race to make vaccines for a dangerous respiratory virus — Millions of people a year are hospitalized by respiratory syncytial virus and tens of thousands die. After decades of failure, four vaccines are now in late-stage trials" ([Nature](#)).

"Investigators dig deep to solve melioidosis mystery" ([CIDRAP](#); Clue spoiler: it was patients, in various rooms, with an aromatherapy spray).

"FDA issues improvement plan focused on modernizing foodborne illness outbreak responses" ([FDA](#)).

"EPA details push to tighten rules for lead in drinking water" ([AP](#)).

### ***Journal Articles***

MMWR: [Dengue Vaccine: Recommendations of the Advisory Committee on Immunization Practices, United States, 2021](#) (17 December 2021)

"This report summarizes the recommendations of the Advisory Committee on Immunization Practices (ACIP) for use of the Dengvaxia vaccine in the United States. The vaccine is a live-attenuated, chimeric tetravalent dengue vaccine built on a yellow fever 17D backbone. Dengvaxia is safe and effective in reducing dengue-related hospitalizations and severe dengue among persons who have had dengue infection in the past. Previous natural infection is important because Dengvaxia is associated with an increased risk for severe dengue in those who experience their first natural infection (i.e., primary infection) after vaccination. Dengvaxia was licensed by the Food and Drug Administration for use among children and adolescents aged 9–16 years (referred to in this report as children). ACIP recommends vaccination with Dengvaxia for children aged 9–16 having evidence of a previous dengue infection and living in areas where dengue is endemic. Evidence of previous dengue infection, such as detection of anti-DENV immunoglobulin G with a highly specific serodiagnostic test, will be required for eligible children before vaccination."

Clin Infect Dis: [Incidence and duration of pharyngeal chlamydia among a cohort of men who have sex with men](#) (10 December 2021)

"Background: The prevalence of pharyngeal chlamydia is low but its incidence and duration are unknown. A high incidence or duration may support the role of pharyngeal chlamydia in sustaining chlamydia transmission.

Methods: From March 2016 to December 2018 we enrolled men who have sex with men (MSM) in a 48-week natural history cohort study in Seattle, Washington. Participants self-

collected pharyngeal specimens weekly. We tested specimens using nucleic acid amplification testing (Aptima Combo-2) at the conclusion of the study. In primary analyses, we defined incident pharyngeal chlamydia as >2 consecutive weeks of a positive pharyngeal specimen. In sensitivity analyses, we defined incident pharyngeal chlamydia as >1 week of a positive specimen. We estimated duration of pharyngeal chlamydia, censoring at loss to follow-up, receipt of antibiotics, or end of study.

Results: 140 participants contributed 70.5 person-years (PY) of follow-up; two (1.4%) had pharyngeal chlamydia at enrollment. In primary analyses, there were 8 pharyngeal chlamydia cases among 6 MSM (incidence=11.4 per 100 PY; 95% confidence interval [CI]=6.0-21.9). In sensitivity analysis, there were 19 cases among 16 MSM (incidence=27.1 per 100 PY; 95% CI=18.5-39.8). The median duration of pharyngeal CT was 6.0 weeks (95% CI=2.0-undefined) in primary analyses and 2.0 weeks (95% CI=1.1-6.0) in sensitivity analysis. Duration was shorter for those with a history of CT compared to those without (3.6 weeks versus 8.7 weeks; P=0.02).

Conclusion: Pharyngeal chlamydia has a low incidence and duration relative to other extragenital sexually transmitted infections. Its contribution to sustained population-level transmission of chlamydia remains unclear."

## Statistics

|                      | <i>Total Cases</i> | <i>Total Deaths</i> | <i>Total Vaccine Doses Administered</i> |
|----------------------|--------------------|---------------------|-----------------------------------------|
| <i>Global</i>        | 273,070,436        | 5,340,120           | 8,626,286,499                           |
| <i>United States</i> | 50,513,437         | 903,652             | not available                           |

[JHU CSSE](#) as of 1000 EDT 17 December 2021

| <i>Virginia</i>  | Total cases (state) | Chesapeake | Hampton | Newport News | Norfolk | Portsmouth | Suffolk | Virginia Beach |
|------------------|---------------------|------------|---------|--------------|---------|------------|---------|----------------|
| Cases            | 1,013,390           | 30,701     | 15,899  | 21,757       | 25,809  | 13,309     | 11,592  | 53,121         |
| Hospitalizations | 39,963              | 1,302      | 587     | 655          | 1,340   | 874        | 697     | 2,631          |
| Deaths           | 15,083              | 375        | 250     | 308          | 363     | 254        | 252     | 586            |

[VA DOH](#) as of 1000 EDT 17 December 2021

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### ***Special Reports and Other Resources***

BPC: Bipartisan Policy Center. Public Health Forward: Modernizing the U.S. Public Health System (December 2021). Link: <https://bipartisanpolicy.org/event/public-health-forward-modernizing-the-u-s-public-health-system/>

CEPA: Center for European Policy Analysis. Ben Dubow, Edward Lucas, and Jake Morris. Jabbed in the Back: Mapping Russian and Chinese Information Operations During COVID-19 (02 December 2021). Link: <https://cepa.org/jabbed-in-the-back-mapping-russian-and-chinese-information-operations-during-covid-19/>

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CSIS: Center for Strategic & International Studies. Rose Butchart. Building Apollo's Arsenal: Acquiring Covid-19's Lessons Learned for Government - Bioeconomy Partnership (14 December 2021). Link: <https://www.csis.org/analysis/building-apollos-arsenal-acquiring-covid-19s-lessons-learned-government-bioeconomy>

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